

Oct-4-Expressing Cells Isolated From Umbilical Cord Matrix Are Multipotential Stem Cells

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We have found an abundant source of mesenchymal stem cells (MSC) in the human umbilical cord matrix (HUCM). These cells proliferate in culture and express markers found in other stem cells. Specifically, HUCM cells express the transcription factors Oct-4 and nanog, which are important for maintaining the undifferentiated, pluripotent state of embryonic stem (ES) cells. Interestingly, expression of Oct-4 and nanog is upregulated by exposure to hypoxia. The Oct-4 expressing cells from umbilical cord matrix are found in the perivascular region of the umbilical cord. They can be differentiated into multiple cell types including neuronal, endothelial, and epithelial cells so are candidates for cell-based therapies. In contrast to ES cells, HUCM cells do not form tumors when injected in immune-compromised mice. Furthermore, these cells are easily accessible compared to bone marrow MSC, are more abundant than the MSC found in cord blood, and lack the ethical considerations of ES cells.

Our previous studies have shown that HUCM cells differentiate into neuronal-like cells that express neuron-specific proteins. HUCM also readily differentiate into endothelial cells when grown in a matrix in the presence of VEGF. Under these conditions they express endothelial markers and lose expression of stem cell markers. Here we show the potential of HUCM cells to incorporate into and heal kidney epithelial cell monolayers after wounding via heat shock, or mechanical disruption. After wounding, the monolayers lose their high transepithelial resistance, as would result from a breakdown of tight junctions. HUCM cells infiltrate into the epithelial monolayer, after which the high resistance and function of the epithelial monolayer are restored. Restoration occurs more rapidly than for monolayers in the absence of HUCM cells. Furthermore, whole-cell patch clamp analysis of HUCM cells retrieved from the monolayers reveals currents found in early kidney tubule that are not seen in the HUCM cells grown in the absence of kidney cells. These findings suggest that HUCM cells are capable of responding to injury-induced environmental cues that target them to wounded kidney epithelium where they differentiate into cells that restore the function of the damaged epithelium *in vitro*. Preliminary studies show that umbilical cord matrix cells can be found in the kidney tubules of rats, 3 weeks after tail vein injections. *In vivo* studies of the effects of HUCM cells in animal models of reperfusion-ischemia injury in the kidney are underway.

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